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* * * * * Welcome to STN International * * * * *

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NEWS 10 OCT 06 STN AnaVist workshops to be held in North America
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NEWS 12 OCT 17 STN(R) AnaVist(TM), Version 1.01, allows the export/download
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NEWS EXPRESS JUNE 13 CURRENT WINDOWS VERSION IS V8.0, CURRENT
MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 13 JUNE 2005

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* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 09:10:52 ON 07 NOV 2005

=> FIL MEDLINE, BIOSIS, EMBASE

COST IN U.S. DOLLARS

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=> s PSMA

L1 841 PSMA

=> s l1 and antibod?

L2 335 L1 AND ANTIBOD?

=> s l2 and isolat?

L3 36 L2 AND ISOLAT?

=> duplicate remove

ENTER L# LIST OR (END):l3

DUPLICATE PREFERENCE IS 'MEDLINE, BIOSIS, EMBASE'

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PROCESSING COMPLETED FOR L3

L4 20 DUPLICATE REMOVE L3 (16 DUPLICATES REMOVED)

=> display l4

ENTER ANSWER NUMBER OR RANGE (1):1-20

ENTER DISPLAY FORMAT (FILEDEFAULT):ti

L4 ANSWER 1 OF 20 MEDLINE on STN

TI The homodimer of prostate-specific membrane antigen is a functional target for cancer therapy.

L4 ANSWER 2 OF 20 MEDLINE on STN

TI Further investigation of the epitope recognized by the new monoclonal antibody 2C9.

L4 ANSWER 3 OF 20 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

TI Session II: Tumor antigens - Prostate cancer antigens and vaccines.

L4 ANSWER 4 OF 20 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

TI Immunotherapy of cancer through expression of truncated tumor or tumor-associated antigen.

L4 ANSWER 5 OF 20 MEDLINE on STN

TI Cloning and expression of extracellular domain of prostate specific membrane antigen in Escherichia coli and preparation of polyclonal antibody.

L4 ANSWER 6 OF 20 MEDLINE on STN DUPLICATE 1

TI In vivo model mimicking natural history of dog prostate cancer using DPC-1, a new canine prostate carcinoma cell line.

L4 ANSWER 7 OF 20 MEDLINE on STN DUPLICATE 2

TI Identification and characterization of circulating prostate carcinoma cells.

L4 ANSWER 8 OF 20 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

TI Molecular and immunohistochemical staging of men with seminal vesicle invasion and negative pelvic lymph nodes at radical prostatectomy.

L4 ANSWER 9 OF 20 MEDLINE on STN DUPLICATE 3

TI Isolation and characterization of monoclonal antibodies

specific for protein conformational epitopes present in prostate-specific membrane antigen (PSMA).

L4 ANSWER 10 OF 20 MEDLINE on STN DUPLICATE 4
TI Comparison of telomerase activity and GSTP1 promoter methylation in ejaculate as potential screening tests for prostate cancer.

L4 ANSWER 11 OF 20 MEDLINE on STN DUPLICATE 5
TI Generation of a baculovirus recombinant prostate-specific membrane antigen and its use in the development of a novel protein biochip quantitative immunoassay.

L4 ANSWER 12 OF 20 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
TI Isolation and characterization of monoclonal antibodies specific for the extracellular domain of prostate specific membrane antigen.

L4 ANSWER 13 OF 20 MEDLINE on STN
TI Expression and purification of prostate-specific membrane antigen in the baculovirus expression system and recognition by prostate-specific membrane antigen-specific T cells.

L4 ANSWER 14 OF 20 MEDLINE on STN
TI PSMA mimotope isolated from phage displayed peptide library can induce PSMA specific immune response.

L4 ANSWER 15 OF 20 MEDLINE on STN DUPLICATE 6
TI Detection of prostatic specific membrane antigen messenger RNA using immunobead reverse transcriptase polymerase chain reaction.

L4 ANSWER 16 OF 20 MEDLINE on STN
TI Identification, purification, and subcellular localization of prostate-specific membrane antigen PSM' protein in the LNCaP prostatic carcinoma cell line.

L4 ANSWER 17 OF 20 MEDLINE on STN DUPLICATE 7
TI Isolation and characterization of monoclonal antibodies specific for the extracellular domain of prostate specific membrane antigen.

L4 ANSWER 18 OF 20 MEDLINE on STN DUPLICATE 8
TI Molecular characterization of human brain N-acetylated alpha-linked acidic dipeptidase (NAALADase).

L4 ANSWER 19 OF 20 MEDLINE on STN DUPLICATE 9
TI Prostate cancer and prostate bed SPECT imaging with ProstaScint: semiquantitative correlation with prostatic biopsy results.

L4 ANSWER 20 OF 20 MEDLINE on STN DUPLICATE 10
TI Measurement of prostate-specific membrane antigen in the serum with a new antibody.

=> display 14

ENTER ANSWER NUMBER OR RANGE (1):1-20

ENTER DISPLAY FORMAT (FILEDEFAULT):all

L4 ANSWER 1 OF 20 MEDLINE on STN
AN 2003507354 MEDLINE
DN PubMed ID: 14583590
TI The homodimer of prostate-specific membrane antigen is a functional target for cancer therapy.
AU Schulke Norbert; Varlamova Olga A; Donovan Gerald P; Ma Dangshe; Gardner

Jason P; Morrissey Donna M; Arrigale Robert R; Zhan Cenchen; Chodera Amy J; Surowitz Kenneth G; Maddon Paul J; Heston Warren D W; Olson William C
 CS Progenics Pharmaceuticals, Inc., and PSMA Development Company, LLC,
 Tarrytown, NY 10591, USA.. nschuelke@progenics.com
 NC CA 91746 (NCI)
 CA 92947 (NCI)
 CA 96075 (NCI)
 SO Proceedings of the National Academy of Sciences of the United States of America, (2003 Oct 28) 100 (22) 12590-5.
 Journal code: 7505876. ISSN: 0027-8424.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 200401
 ED Entered STN: 20031030
 Last Updated on STN: 20040106
 Entered Medline: 20040105
 AB Prostate-specific membrane antigen (PSMA) is a type 2 integral membrane glycoprotein that serves as an attractive target for cancer immunotherapy by virtue of its abundant and restricted expression on the surface of prostate carcinomas and the neovasculature of most other solid tumors. However, relatively little is known about the molecular structure of this target. Here, we report that PSMA is expressed on tumor cells as a noncovalent homodimer. A truncated PSMA protein, lacking transmembrane and cytoplasmic domains, also formed homodimers, indicating that the extracellular domain is sufficient for dimerization. PSMA dimers but not monomers displayed a native conformation and possessed high-level carboxypeptidase activity. A unique dimer-specific epitope was identified by using one of a panel of novel mAbs. When used to immunize animals, dimer but not monomer elicited antibodies that efficiently recognized PSMA-expressing tumor cells. These findings on PSMA structure and biology may have important implications for active and passive immunotherapy of prostate and other cancers.
 CT Check Tags: Male
 3T3 Cells
 Animals
 Antibodies, Monoclonal
 *Antigens, Surface: CH, chemistry
 Antigens, Surface: GE, genetics
 Antigens, Surface: IP, isolation & purification
 *Antineoplastic Agents: TO, toxicity
 CHO Cells
 Cell Membrane: DE, drug effects
 Cell Membrane: EN, enzymology
 Dimerization
 *Glutamate Carboxypeptidase II: CH, chemistry
 Glutamate Carboxypeptidase II: GE, genetics
 Glutamate Carboxypeptidase II: IP, isolation & purification
 Hamsters
 Humans
 Mice
 Prostatic Neoplasms: EN, enzymology
 Recombinant Proteins: CH, chemistry
 Recombinant Proteins: IP, isolation & purification
 Research Support, U.S. Gov't, P.H.S.
 Transfection
 Tumor Cells, Cultured
 CN 0 (Antibodies, Monoclonal); 0 (Antigens, Surface); 0 (Antineoplastic Agents); 0 (Recombinant Proteins); EC 3.4.17.21 (Glutamate Carboxypeptidase II); EC 3.4.17.21 (glutamate carboxypeptidase II, human)
 L4 ANSWER 2 OF 20 MEDLINE on STN

AN 2003419045 MEDLINE
 DN PubMed ID: 12887366
 TI Further investigation of the epitope recognized by the new monoclonal antibody 2C9.
 AU Kato Keitaro; Yoshikawa Kazuhiro; Taki Tomohiro; Shitara Kenya; Nakamura Kazuyasu; Hirota Maiko; Hanai Nobuo; Nakamura Kogenta; Kokubo Hiroto; Mitsui Kenji; Yamada Yoshiaki; Honda Nobuaki; Ueda Ryuzo; Saga Shinsuke; Fukatsu Hidetoshi
 CS Department of Urology, Aichi Medical University School of Medicine, Nagakute, Aichi, Japan.
 SO International journal of urology : official journal of the Japanese Urological Association, (2003 Aug) 10 (8) 439-44.
 Journal code: 9440237. ISSN: 0919-8172.
 CY Australia
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 200401
 ED Entered STN: 20030909
 Last Updated on STN: 20040116
 Entered Medline: 20040115
 AB OBJECTIVE: We established a new monoclonal antibody (2C9) that reacted with prostate tissue. The immunohistochemical reactivity of this antibody is similar to anti-prostate-specific membrane antigen (PSMA). Herein, we report the antigenic determinant of 2C9 antibody. METHODS: The reactivity of the antibody was characterized by immunohistochemical staining and the antigen target was characterized by amino acid sequencing after immuno-affinity purification from an LNCaP cell lysate and cloning of a cDNA using a mammalian expression cDNA cloning system. RESULTS: The amino acid and nucleotide sequences for the antigen molecule recognized with 2C9 monoclonal antibody demonstrated identity with PSMA. CONCLUSION: The target molecule of the 2C9 monoclonal antibody is PSMA, pointing to future diagnostic and therapeutic applications.
 CT Check Tags: Male
 Amino Acid Sequence
 Antibodies, Monoclonal: CH, chemistry
 *Antibodies, Monoclonal: IM, immunology
 Antibodies, Monoclonal: IP, isolation & purification
 Base Sequence
 Blotting, Northern
 Cell Line, Tumor: IM, immunology
 Cell Line, Tumor: ME, metabolism
 Clone Cells: IM, immunology
 DNA, Complementary: GE, genetics
 DNA, Complementary: IP, isolation & purification
 Epitope Mapping: MT, methods
 *Epitopes: AN, analysis
 Humans
 Molecular Sequence Data
 Molecular Weight
 Prostate: CH, chemistry
 Prostate: IM, immunology
 *Prostate-Specific Antigen: AN, analysis
 Prostate-Specific Antigen: CH, chemistry
 Prostatic Neoplasms: CH, chemistry
 Prostatic Neoplasms: GE, genetics
 *Prostatic Neoplasms: IM, immunology
 Research Support, Non-U.S. Gov't
 Sequence Analysis, Protein
 Tumor Markers, Biological: GE, genetics
 *Tumor Markers, Biological: IM, immunology
 CN 0 (Antibodies, Monoclonal); 0 (DNA, Complementary); 0 (Epitopes); 0 (Tumor Markers, Biological); EC 3.4.21.77 (Prostate-Specific

Antigen)

L4 ANSWER 3 OF 20 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
AN 2005387607 EMBASE
TI Session II: Tumor antigens - Prostate cancer antigens and vaccines.
AU Salgaller M.L.; Elgamal A.-A.; Bosch M.; Lodge A.; Shankar G.; Boynton A.; Belldegrün A.; Logothetis C.; Papandreou C.
CS Dr. M.L. Salgaller, Northwest Biotherapeutics, Inc., Seattle, WA, United States
SO Cancer Immunology, Immunotherapy, (2003) Vol. 52, No. SUPPL. 1, pp. S8-S9+S27.
ISSN: 0340-7004 CODEN: CIIMDN
CY Germany
DT Journal; Conference Article
FS 016 Cancer
026 Immunology, Serology and Transplantation
028 Urology and Nephrology
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English
ED Entered STN: 20050915
Last Updated on STN: 20050915
AB The clinical development of prostate cancer vaccines presents several challenges. Reagents are more limited and difficult to obtain as compared with other tumor types. The advanced age of the patient population presents the researcher with subjects having diminished immune systems and who are often less willing to undergo procedures for research purposes. Consequently, the majority of research has involved those cancers for which tumor and immune cells are readily available. Despite these hurdles, new and novel approaches are improving the poor overall survival rates through the development of antigen-based treatment options. These efforts are particularly important in the realm of hormone-refractory prostate cancer (HRPC), since no therapy exists with significant clinical impact. This is a major issue for the 36,000 men who will die from the disease annually, despite transient responses to secondary treatment such as hormone ablation therapy. During the past few years, candidate target antigens for experimental vaccines have been identified in several laboratories. These include oncogenes, overexpressed proteins, and carbohydrates. Three of the furthest in clinical development are well-established clinical markers of prostate cancer: prostate-specific membrane antigen (PSMA), prostate-specific antigen (PSA), and prostatic acid phosphatase (PAP). Following conclusive preclinical evidence indicating that the human body responds immunologically to prostate antigens, clinical trials have been underway for many years with PSMA, PSA, and PAP as targets. We investigated the capacity of a vaccine composed of autologous dendritic cells (DC), pulsed ex vivo with recombinant PSMA (rPS-MA), to safely generate clinically meaningful antitumor immune responses in HRPC patients. In 2000 and 2001, 32 patients with metastatic or non-metastatic HRPC were enrolled in a phase I/II clinical trial. Their peripheral blood mononuclear cells were isolated by leukapheresis, matured to DC by in vitro culture with maturation factors (GM-CSF, IL-4, and inactivated BCG) for up to 7 days, followed by rPSMA loading and harvesting of the vaccine. Patients received four intradermal treatments of 5, 10, or 20-million rPSMA-loaded mature DC at monthly intervals, followed by up to a total of 6 months of observation. Measurement of serum anti-PSMA antibodies, PSMA-stimulated lymphocyte proliferation, and delayed-type hypersensitivity (DTH) skin testing were carried out before, during, and after vaccination. Clinical responses were assessed by CT/bone scans and hematochemical laboratory tests, including PSA levels. More than 140 total vaccine injections were well tolerated; no clinical signs of autoimmunity or serious adverse events were observed. Overall, 54% of

patients achieved stability of their disease at >6 months follow-up, as assessed by radiographic criteria, and 83% of patients had a PSMA-specific immune response, 92% of patients with stable disease had a PSMA-specific immune response, and 46% of patients had a decrease in PSA velocity. Compared to baseline, 93% of 27 evaluable patients converted to DTH-positive against the BCG component of the vaccine. Due to these promising initial findings we have initiated a double-blind, placebo-controlled phase III clinical trial. .COPYRGT. 2002 Northwest Biotherapeutics, Inc. All rights reserved.

CT Medical Descriptors:

*prostate cancer: DT, drug therapy
prostatectomy
cancer surgery
bone metastasis
cancer cell culture
T lymphocyte
medical research
cancer chemotherapy
immune response
cancer survival
quality of life
dendritic cell
peripheral blood mononuclear cell
skin irritation: SI, side effect
injection site reaction: SI, side effect
headache: SI, side effect
fatigue: SI, side effect
human

clinical trial

conference paper

priority journal

Drug Descriptors:

*tumor antigen
*cancer vaccine: AE, adverse drug reaction
*cancer vaccine: CT, clinical trial
*cancer vaccine: DT, drug therapy
tumor rejection antigen
tumor suppressor protein
prostate antigen
acid phosphatase prostate isoenzyme
prostate specific antigen
prostate specific membrane antigen: DT, drug therapy
prostate specific membrane antigen: DL, intradermal drug administration
prostate specific membrane antigen: PD, pharmacology
recombinant antigen: DT, drug therapy
recombinant antigen: DL, intradermal drug administration
recombinant antigen: PD, pharmacology
dendritic cell vaccine: AE, adverse drug reaction
dendritic cell vaccine: CT, clinical trial
dendritic cell vaccine: DT, drug therapy

L4 ANSWER 4 OF 20 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 2002:338468 BIOSIS

DN PREV200200338468

TI Immunotherapy of cancer through expression of truncated tumor or
tumor-associated antigen.

AU Mincheff, Milcho S. [Inventor, Reprint author]; Loukinov, Dmitri I.
[Inventor]; Zoubak, Serguei [Inventor]

CS Rockville, MD, USA

ASSIGNEE: American Foundation for Biological Research, Inc., Rockville,
MD, USA

PI US 6387888 20020514

SO Official Gazette of the United States Patent and Trademark Office Patents,
(May 14, 2002) Vol. 1258, No. 2. <http://www.uspto.gov/web/menu/patdata.htm>

1. e-file.

CODEN: OGUPE7. ISSN: 0098-1133.

DT Patent

LA English

ED Entered STN: 12 Jun 2002

Last Updated on STN: 12 Jun 2002

AB DNA constructs for truncated forms of cancer-specific or cancer associated antigens are included in plasmid or viral expression vectors. The rationale to use constructs for truncated and not for full-size molecules is to eliminate side effects (toxicity, signal transduction etc.) arising from expressed proteins and/or, in cases where such molecules are expressed on the membrane, secreted, or released in the extracellular environment, to prevent formation of antibodies against them. The extracellular portion of the human prostate specific membrane specific antigen (XC-PSMA) has been cloned. Patients were treated either by injection of DNA coding for XC-PSMA in a mammalian expression vector under the CMV promoter or/and by a replication-defective adenoviral vector (Ad5) that contains an expression cassette for the XC-PSMA. In a third method dendritic cells are isolated from a patient and are treated by exposure to the plasmid or adenovirus used in the previous two treatments. The dendritic cells are then injected into the patient. In some patients, the progression of metastatic prostate cancer is retarded or stopped.

NCL 514044000

CC Pathology - Therapy 12512

Neoplasms - Pathology, clinical aspects and systemic effects 24004

Neoplasms - Therapeutic agents and therapy 24008

IT Major Concepts

Methods and Techniques; Oncology (Human Medicine, Medical Sciences)

IT Methods & Equipment

cancer immunotherapy: therapeutic method

L4 ANSWER 5 OF 20 MEDLINE on STN

AN 2002240387 MEDLINE

DN PubMed ID: 11977596

TI Cloning and expression of extracellular domain of prostate specific membrane antigen in Escherichia coli and preparation of polyclonal antibody.

AU Ye Chuan-Zhong; Zhao Xu-Dong; Zhang Fang-Lin; Lin Zhen; Xu Ming; Zhang Yong-Kang; Chen Chang-Qing

CS Department of Urology, Zhongshan Hospital, Medical Center of Fudan University, Shanghai 200032, China.. chuanzhong@mycity.com.cn

SO Sheng wu gong cheng xue bao = Chinese journal of biotechnology, (2002 Jan) 18 (1) 35-9.

Journal code: 9426463. ISSN: 1000-3061.

CY China

DT Journal; Article; (JOURNAL ARTICLE)

LA Chinese

FS Priority Journals

EM 200206

ED Entered STN: 20020430

Last Updated on STN: 20020625

Entered Medline: 20020624

AB Human Prostate Specific Membrane Antigen(PSMA) cDNA was amplified using total RNA extracted from prostate carcinoma tissue by RT-PCR. The cDNA fragment of extracellular domain of PSMA (edPSMA) gene was amplified by PCR and cloned into expression vector pMAL-c2x. Sequence analysis of both PSMA and edPSMA revealed identity to the GenBank reported. The edPSMA was expressed in E. coli as part of a fusion protein with MBP as the induction of IPTG. Western blot analysis showed the recombinant protein could react with PSMA monocloned antibodies 4G5. MBP-edPSMA fusion protein were purified by amylose resin affinity chromatography and showed to be homogeneity in SDS-PAGE(120 kD). BALB/C mice were immunized with the

purified protein for the preparation of polyclonal antibody. The polyclonal antibody, which had a title of 1:12,800, were indicated the specificity to prostate tissue.

CT Animals
 *Antibodies: IM, immunology
 Antibody Formation
 *Antigens, Surface
 *Carboxypeptidases: BI, biosynthesis
 Carboxypeptidases: GE, genetics
 Carboxypeptidases: IM, immunology
 Carboxypeptidases: IP, isolation & purification
 Chromatography, Affinity: MT, methods
 Cloning, Molecular
 DNA, Complementary: GE, genetics
 English Abstract
 Escherichia coli: GE, genetics
 *Gene Expression
 Genetic Vectors
 Glutamate Carboxypeptidase II
 Humans
 Mice
 Mice, Inbred BALB C
 Protein Structure, Tertiary: GE, genetics
 Protein Structure, Tertiary: PH, physiology
 Recombinant Fusion Proteins: BI, biosynthesis
 Recombinant Fusion Proteins: GE, genetics
 Recombinant Fusion Proteins: IM, immunology
 Recombinant Fusion Proteins: IP, isolation & purification
 Research Support, Non-U.S. Gov't
 Reverse Transcriptase Polymerase Chain Reaction: IS, instrumentation

CN 0 (Antibodies); 0 (Antigens, Surface); 0 (DNA, Complementary); 0
(Genetic Vectors); 0 (Recombinant Fusion Proteins); EC 3.4.-
(Carboxypeptidases); EC 3.4.17.21 (Glutamate Carboxypeptidase II); EC
3.4.17.21 (glutamate carboxypeptidase II, human)

L4 ANSWER 6 OF 20 MEDLINE on STN DUPLICATE 1
AN 2001156016 MEDLINE
DN PubMed ID: 11170126
TI In vivo model mimicking natural history of dog prostate cancer using
 DPC-1, a new canine prostate carcinoma cell line.
AU Anidjar M; Villette J M; Devauchelle P; Delisle F; Cotard J P; Billotey C;
 Cochand-Priollet B; Copin H; Barnoux M; Triballeau S; Rain J D; Fiet J;
 Teillac P; Berthon P; Cussenot O
CS Centre de Recherche pour les Pathologies Prostatiques, Evry, France.
SO Prostate, (2001 Jan 1) 46 (1) 2-10.
 Journal code: 8101368. ISSN: 0270-4137.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200103
ED Entered STN: 20010404
 Last Updated on STN: 20010404
 Entered Medline: 20010322

AB BACKGROUND: Dog prostate cancer is usually considered to be highly
 relevant to human prostate cancer. We report the isolation of a
 new canine prostate cancer epithelial cell line designated DPC-1.
 METHODS: Primary cultures were established from a canine poorly
 differentiated prostatic adenocarcinoma. Population doubling time was
 determined by counting nuclei after cell lysis. Tumorigenicity was
 assessed in nude mice and in one adult immunodeficient dog.
 Immunoscintigraphy was performed in both models using a monoclonal
 antibody (mAb) raised against the [44-62] sequence of human
 PSMA. RESULTS: DPC-1 cells have a rapid growth in vitro (doubling

time, 27 hr) which is not stimulated by androgens. In addition, DPC-1 displays immunoreactivity to human PSA and PSMA. DPC-1 was found to be highly tumorigenic not only in nude mice but also for the first time after orthotopic seeding in an immunodeficient dog. This allograft mimicked, in a compressed form, the aggressive biological behavior of spontaneous dog prostate adenocarcinoma. Immunoscintigraphy using a (131)Iodine-labeled PSMA mAb clearly visualized induced tumors in nude mice and in the dog allograft. CONCLUSIONS: This study suggests that DPC-1 may constitute a powerful model for assessing new diagnostic and/or therapeutic tools in the management of prostate cancer. Copyright 2001 Wiley-Liss, Inc.

CT Check Tags: Male
*Adenocarcinoma: PA, pathology
Adenocarcinoma: RI, radionuclide imaging
Animals
Antibodies, Monoclonal
Dihydrotestosterone: CH, chemistry
Disease Models, Animal
Dogs
Humans
Immunohistochemistry
Iodine Radioisotopes
Mice
Mice, Nude
Microscopy, Fluorescence
Microscopy, Phase-Contrast
*Prostatic Neoplasms: PA, pathology
Prostatic Neoplasms: RI, radionuclide imaging
*Tumor Cells, Cultured: PA, pathology
Tumor Cells, Cultured: RI, radionuclide imaging
RN 521-18-6 (Dihydrotestosterone)
CN 0 (Antibodies, Monoclonal); 0 (Iodine Radioisotopes)

L4 ANSWER 7 OF 20 MEDLINE on STN DUPLICATE 2
AN 2000329861 MEDLINE
DN PubMed ID: 10870062
TI Identification and characterization of circulating prostate carcinoma cells.
AU Wang Z P; Eisenberger M A; Carducci M A; Partin A W; Scher H I; Ts'o P O
CS Cell Works Inc., Baltimore, MD 21227-2349, USA.
SO Cancer, (2000 Jun 15) 88 (12) 2787-95.
Journal code: 0374236. ISSN: 0008-543X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200007
ED Entered STN: 20000728
Last Updated on STN: 20000728
Entered Medline: 20000719
AB BACKGROUND: Analysis of prostate carcinoma cells isolated from the peripheral blood suggested a classification based on three categories. METHODS: Centrifugation density gradients and magnetic cell sorting were used to isolate circulating prostate carcinoma cells from peripheral blood. Immunocytochemistry staining and fluorescent in situ hybridization allowed characterization of isolated cancer cells. RESULTS: Terminal cells can be divided into 3 classes: 1) large, buoyant, fragile cells with a large nucleus that were captured in a 1.068 g/mL gradient; 2) enucleate cells (4, 6-diamidino-2-phenylindole [DAPI] negative) that were positive for cytokeratin and PSMA antibodies; and 3) cellular debris exhibiting cytokeratin and PSMA positive staining as well as nuclear debris identified by DAPI staining, which included cytoplasmic debris. Growing cells also exhibited three morphologic characteristics: those possessing stem

cell-like morphology and characteristics such as small size, high density, developed cytokeratin systems, PSMA expression, and aneuploidy; those in M phase; and cell clusters. The majority of isolated cells exhibited intermediate characteristics and thus comprised the third group of circulating cancer cells. CONCLUSIONS: Although the significance of the cluster remains undetermined, observation suggests that the cluster has the ability to circulate as a microtumor and subsequently arrest in the small veins and capillaries. It is hypothesized that the clusters could escape certain facets of immune surveillance and possibly gain a selective growth advantage over single cells in a distant site. Further hypothesis proposes that arrested cells recruit growth-promoting nutrients, which would result in the invasion of local blood vessels and vascularization.

Copyright 2000 American Cancer Society.

CT Check Tags: Male

Aged

Aged, 80 and over

Cell Division

Humans

Immunohistochemistry

In Situ Hybridization, Fluorescence

Middle Aged

*Neoplasm Circulating Cells: CL, classification

Neoplasm Circulating Cells: PA, pathology

Neoplasm Circulating Cells: UL, ultrastructure

Neoplasm Metastasis

Prognosis

*Prostatic Neoplasms: PA, pathology

Research Support, Non-U.S. Gov't

L4 ANSWER 8 OF 20 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

AN 2001008412 EMBASE

TI Molecular and immunohistochemical staging of men with seminal vesicle invasion and negative pelvic lymph nodes at radical prostatectomy.

AU Potter S.R.; Mangold L.A.; Shue M.J.; Taylor D.C.; Lecksell K.L.; Epstein J.I.; Walsh P.C.; Partin A.W.

CS Dr. A.W. Partin, Johns Hopkins Hospital, Department of Urology, Marburg-205A, 600 North Wolfe Street, Baltimore, MD 21287-2101, United States. apartin@jhmi.edu

SO Cancer, (15 Dec 2000) Vol. 89, No. 12, pp. 2577-2586.

Refs: 34

ISSN: 0008-543X CODEN: CANCAR

CY United States

DT Journal; Article

FS 005 General Pathology and Pathological Anatomy

016 Cancer

028 Urology and Nephrology

029 Clinical Biochemistry

LA English

SL English

ED Entered STN: 20010119

Last Updated on STN: 20010119

AB BACKGROUND. Patients with seminal vesicle invasion (SVI) at radical retropubic prostatectomy (RRP) have a poor prognosis. Routine microscopic examination of pelvic lymph nodes (LNs) can miss small metastases and, thereby, confuse tumor staging and clinical decision-making. The authors used immunohistochemical and molecular methods to examine archival paraffin-embedded LNs of men who had undergone RRP for clinically localized prostate carcinoma and who had tumors demonstrating SVI and negative LNs at surgery. METHODS. Between June 1982 and June 1997, 2151 consecutive men underwent RRP for clinically localized prostate carcinoma. Of these, 109 (5.1%) tumors had SVI with negative LNs. The actuarial likelihood of having a tumor that was undetectable by testing

prostate-specific antigen (PSA) 5 and 10 years after surgery was 45% and 29%, respectively, for men with isolated SVI. Archival LN specimens were available for 102 men who had isolated SVI. Reverse transcription polymerase chain reaction (RT-PCR) was performed for PSA and prostate-specific membrane antigen (PSMA). All specimens were examined concurrently by immunohistochemistry (IHC). RESULTS: Careful reevaluation of pelvic LNs demonstrated metastases in 9 (8.8%) men originally classified as metastasis-free. Reevaluation by hematoxylin and eosin (H&E) staining identified three previously unrecognized cases of LN metastases. IHC identified six cases, three of which were missed by H&E. RT-PCR identified four cases, three of which were not revealed by other methods. CONCLUSIONS. The poor prognosis of patients with SVI does not seem due to occult LN metastases. The low yield of unsuspected foci of prostate carcinoma in the LNs of men with SVI and negative LNs by routine staging does not justify IHC or molecular examination to find occult carcinoma. .COPYRGHT. 2000 American Cancer Society.

CT Medical Descriptors:

*prostate carcinoma: SU, surgery
 *cancer staging
 *lymph node metastasis: CO, complication
 *lymph node metastasis: DI, diagnosis
 immunohistochemistry
 molecular biology
 seminal vesicle disease: DI, diagnosis
 tumor localization
 reverse transcription polymerase chain reaction
 intermethod comparison
 antibody labeling

human

male

major clinical study

controlled study

human cell

article

priority journal

Drug Descriptors:

hematoxylin: EC, endogenous compound

eosin: EC, endogenous compound

RN (hematoxylin) 517-28-2; (eosin) 17372-87-1, 51395-88-1, 548-26-5

L4 ANSWER 9 OF 20 MEDLINE on STN

DUPLICATE 3

AN 2001043108 MEDLINE

DN PubMed ID: 10952413

TI Isolation and characterization of monoclonal antibodies

specific for protein conformational epitopes present in prostate-specific membrane antigen (PSMA).

AU Tino W T; Huber M J; Lake T P; Greene T G; Murphy G P; Holmes E H

CS Northwest Biotherapeutics, Inc., Seattle, Washington 98134, USA.

SO Hybridoma, (2000 Jun) 19 (3) 249-57.

Journal code: 8202424. ISSN: 0272-457X.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 200012

ED Entered STN: 20010322

Last Updated on STN: 20010322

Entered Medline: 20001207

AB Prostate-specific membrane antigen (PSMA) is a 750-amino acid glycoprotein highly expressed in malignant prostate tissues. PSMA reacts with the murine monoclonal antibody 7E11.C5, whose binding epitope has been mapped to the N-terminal of the protein distributed on the cytoplasmic side of the plasma membrane. We have

developed murine monoclonal antibodies specific for extracellular epitopes of PSMA. Three of these antibodies--1G9, 3C6, and 4D4--display distinct binding properties consistent with their recognition of conformational epitopes within native PSMA. Results indicate this panel of antibodies binds to native full-length PSMA, but not to fusion proteins containing portions of the linear sequence of the protein. Antibody binding is greatly reduced upon heat denaturation of native PSMA, and these antibodies do not detect PSMA by Western blot. Immunoprecipitation experiments demonstrate the ability of each to bind to full-length PSMA as well as PSM', a form of the protein missing the first 57 amino acids. These results indicate each antibody is specific for an epitope within the extracellular domain, a region spanning residues 44-750. Flow cytometric experiments indicate strong specific binding to live LNCaP cells. Antibody inhibition studies demonstrate that these antibodies recognize at least two distinct epitopes. Taken together, the results demonstrate that these antibodies are specific for native protein conformational epitopes within the extracellular domain. Their properties, in particular strong binding to live cancer cells, make them ideal candidates that are clearly superior to linear sequence epitope specific antibodies for in vivo applications.

CT Check Tags: Female; Male

Animals

*Antibodies, Monoclonal: CH, chemistry

*Antibodies, Monoclonal: IP, isolation & purification

Antibodies, Monoclonal: ME, metabolism

*Antibody Specificity

*Antigens, Surface

Blotting, Western

Carboxypeptidases: CH, chemistry

*Carboxypeptidases: IM, immunology

Carboxypeptidases: ME, metabolism

Enzyme-Linked Immunosorbent Assay

Epitopes: AN, analysis

*Epitopes: IM, immunology

Glutamate Carboxypeptidase II

Humans

Hybridomas

Immunoglobulin G: AN, analysis

Mice

Mice, Inbred A

Mice, Inbred BALB C

Organ Specificity: IM, immunology

Prostate: EN, enzymology

*Prostate: IM, immunology

Prostatic Neoplasms: IM, immunology

Protein Conformation

Protein Denaturation

Research Support, Non-U.S. Gov't

Tumor Cells, Cultured

CN 0 (Antibodies, Monoclonal); 0 (Antigens, Surface); 0 (Epitopes);
0 (Immunoglobulin G); EC 3.4.- (Carboxypeptidases); EC 3.4.17.21
(Glutamate Carboxypeptidase II); EC 3.4.17.21 (glutamate carboxypeptidase
II, human)

L4 ANSWER 10 OF 20 MEDLINE on STN

DUPLICATE 4

AN 2001031762 MEDLINE

DN PubMed ID: 10970725

TI Comparison of telomerase activity and GSTP1 promoter methylation in
ejaculate as potential screening tests for prostate cancer.

AU Suh C I; Shanafelt T; May D J; Shroyer K R; Bobak J B; Crawford E D;
Miller G J; Markham N; Glode L M

CS University of Colorado Health Sciences Center and University of Colorado
Cancer Center, Denver, CO 80262, USA.

SO Molecular and cellular probes, (2000 Aug) 14 (4) 211-7.
Journal code: 8709751. ISSN: 0890-8508.

CY ENGLAND: United Kingdom

DT (EVALUATION STUDIES)
Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 200011

ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001120

AB New diagnostic tools are needed for the early detection of prostatic
cancer. The molecular detection of prostate cancer cells in ejaculates
was evaluated using complementary PCR-based methods. LNCaP cells, a cell
line derived from prostatic carcinoma, were spiked into normal seminal
ejaculates and the prostatic epithelial component of the specimens was
isolated by immunomagnetic bead sorting, using a monoclonal
antibody to prostate-specific membrane antigen (PSMA).
Ejaculates from nine patients with a recent diagnosis of prostate cancer
were processed in a similar fashion, using LNCaP-spiked aliquots as an
internal positive control. Telomerase expression was evaluated by the
telomeric repeat amplification protocol (TRAP) and glutathione
S-transferase gene promoter (GSTP1) hypermethylation was evaluated by
methylation-sensitive restriction endonuclease digestion and PCR
amplification. Telomerase activity was detected in LNCaP cells recovered
from normal seminal ejaculates but was not found in all nine samples from
patients with prostate cancer. The sensitivity of GSTP1 analysis was
similar to telomerase analysis for the detection of LNCaP cells from
normal ejaculate samples but was positive in ejaculates from four out of
nine patients with prostate cancer. GSTP1 DNA methylation status is more
sensitive than telomerase analysis for the detection of malignant cells in
seminal ejaculates from patients with prostate cancer.
Copyright 2000 Academic Press.

CT Check Tags: Comparative Study; Male
DNA Methylation
Ejaculation
*Glutathione Transferase: GE, genetics
Humans
*Isoenzymes: GE, genetics
Mass Screening: MT, methods
Promoter Regions (Genetics)
*Prostatic Neoplasms: DI, diagnosis
*Prostatic Neoplasms: GE, genetics
Reference Values
Research Support, Non-U.S. Gov't
Spermatozoa: PH, physiology
Telomerase: AN, analysis
*Telomerase: ME, metabolism
Tumor Cells, Cultured

CN 0 (Isoenzymes); EC 2.5.1.18 (Glutathione Transferase); EC 2.5.1.18
(glutathione S-transferase pi); EC 2.7.7.- (Telomerase)

L4 ANSWER 11 OF 20 MEDLINE on STN DUPLICATE 5

AN 2000391693 MEDLINE

DN PubMed ID: 10833385

TI Generation of a baculovirus recombinant prostate-specific membrane antigen
and its use in the development of a novel protein biochip quantitative
immunoassay.

AU Xiao Z; Jiang X; Beckett M L; Wright G L Jr

CS Department of Microbiology and Molecular Cell Biology, Eastern Virginia
Medical School, Norfolk, Virginia 23507, USA.

NC CA85067 (NCI)

SO Protein expression and purification, (2000 Jun) 19 (1) 12-21.
Journal code: 9101496. ISSN: 1046-5928.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 200008

ED Entered STN: 20000824
Last Updated on STN: 20000824
Entered Medline: 20000814

AB Prostate-specific membrane antigen (PSMA) is a 100-kDa transmembrane glycoprotein identified by the monoclonal antibody 7E11-C5.3 from the human prostate tumor cell line LNCaP. Because of its significant upregulation in androgen refractory and metastatic prostate cancers, PSMA may be a useful prognostic biomarker and a target for developing novel therapeutic strategies. However, the lack of abundant pure PSMA protein and the low efficacy in immunoaffinity isolation from LNCaP cells have hampered the development of clinical assays. In order to obtain a renewable and reliable source of pure antigen, we used the baculovirus/insect cell system to express and purify a recombinant PSMA. A recombinant baculovirus containing a 6x histidine-tagged PSMA gene was generated, from which rPSMA was expressed and purified using cobalt-chelating affinity chromatography. The purity and correct molecular size of rPSMA were demonstrated by gel electrophoresis and mass spectrometry. Glycosidase digestions showed that the oligosaccharides on rPSMA are primarily N-linked high-mannose type. Although the glycosylation is different from the native PSMA, it did not affect the immunoreactivity of rPSMA to antibodies specific for either the intra- or the extracellular domains of PSMA. Finally, the purified rPSMA was successfully used to develop a quantitative PSMA immunoassay using the novel ProteinChip surface-enhanced laser desorption/ionization mass spectrometry technology. Copyright 2000 Academic Press.

CT Animals
Antibodies, Monoclonal
Antigens, Neoplasm: BL, blood
*Antigens, Neoplasm: IP, isolation & purification
Antigens, Neoplasm: ME, metabolism
*Antigens, Surface
Baculoviridae: GE, genetics
Blotting, Western
Carboxypeptidases: BL, blood
*Carboxypeptidases: IP, isolation & purification
Carboxypeptidases: ME, metabolism
Cell Line
Chromatography, Affinity
Genetic Vectors
Glutamate Carboxypeptidase II
Glycosylation
Humans
Immunoassay: MT, methods
Lepidoptera: CY, cytology
Recombinant Fusion Proteins: BL, blood
*Recombinant Fusion Proteins: IP, isolation & purification
Recombinant Fusion Proteins: ME, metabolism
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, P.H.S.
Spectrometry, Mass, Matrix-Assisted Laser Desorption-Ionization: MT, methods

CN 0 (Antibodies, Monoclonal); 0 (Antigens, Neoplasm); 0 (Antigens, Surface); 0 (Genetic Vectors); 0 (Recombinant Fusion Proteins); EC 3.4.- (Carboxypeptidases); EC 3.4.17.21 (Glutamate Carboxypeptidase II); EC 3.4.17.21 (glutamate carboxypeptidase II, human)

L4 ANSWER 12 OF 20 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

AN 1999359102 EMBASE

TI Isolation and characterization of monoclonal antibodies specific for the extracellular domain of prostate specific membrane antigen.

AU Murphy G.P.; Greene T.G.; Tino W.T.; Boynton A.L.; Holmes E.H.

CS G.P. Murphy, Northwest Hospital, Pacific Northwest Cancer Foundation, Northwest Biotherapeutics, Seattle, WA, United States

SO Journal of Urology, (1999) Vol. 160, No. 6 II, pp. 2396-2401.

Refs: 27

ISSN: 0022-5347 CODEN: JOURAA

CY United States

DT Journal; Article

FS 016 Cancer
026 Immunology, Serology and Transplantation
028 Urology and Nephrology
037 Drug Literature Index

LA English

SL English

ED Entered STN: 19991029
Last Updated on STN: 19991029

AB Purpose: Monoclonal antibodies specific for protein epitopes of prostate specific membrane antigen (PSMA) expressed on the external surface of prostatic epithelial cells were prepared to provide material for use in the diagnosis or treatment of prostatic cancer. Materials and Methods: Mice were immunized with LNCaP cell membranes followed by purified PSMA before fusion. Hybridomas were screened by reactivity with purified PSMA. Resulting antibodies were characterized by enzyme-linked immunosorbent assay, Western blot and fluorescence-activated cell sorter analyses. Results: Monoclonal antibody producing hybridomas designated 3E11, 3C2, 4E10-1.14, 3C9 and 1G3 were obtained which displayed specificities for differing regions of the extracellular domain of the PSMA protein. These antibodies reacted strongly with PSMA from multiple sources and specifically stained unfixed PSMA expressing cells by flow cytometric analysis. Conclusions: The antibodies obtained displayed strong reactivity and specificity for extracellular epitopes of PSMA. These antibodies will have value in future diagnostic and therapeutic applications focusing on PSMA as a target antigen.

CT Medical Descriptors:
*prostate cancer: DT, drug therapy
*antibody production
antigen expression
prostate epithelium
hybridoma
cancer screening
enzyme linked immunosorbent assay
immunoblotting
fluorescence activated cell sorter
flow cytometry
nonhuman
mouse
controlled study
animal cell
article
priority journal
Drug Descriptors:
*monoclonal antibody: DT, drug therapy
*prostate specific antigen: EC, endogenous compound

L4 ANSWER 13 OF 20 MEDLINE on STN

AN 1999332515 MEDLINE
 DN PubMed ID: 10404436
 TI Expression and purification of prostate-specific membrane antigen in the baculovirus expression system and recognition by prostate-specific membrane antigen-specific T cells.
 AU Lodge P A; Childs R A; Monahan S J; McLean J G; Sehgal A; Boynton A L; Salgaller M L; Murphy G P
 CS Northwest Biotherapeutics, L.L.C., WA 98125, USA.
 SO Journal of immunotherapy (Hagerstown, Md. : 1997), (1999 Jul) 22 (4) 346-55.
 Journal code: 9706083. ISSN: 1524-9557.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199909
 ED Entered STN: 19991012
 Last Updated on STN: 19991012
 Entered Medline: 19990928
 AB Antigen-specific immunotherapy of cancer depends on a consistent source of well-defined protein antigen. Production of recombinant protein offers the obvious solution to this problem but few comparisons of recombinant and native proteins in cellular immune assays have been reported. We report expression of a putative immunotherapy antigen, prostate-specific membrane antigen (PSMA), in insect cells using a baculovirus vector. T cells stimulated with recombinant PSMA or native PSMA derived from the LNCaP cell line recognized both native PSMA and recombinant, baculoviral PSMA. These data indicate that PSMA produced in Sf9 cells is immunologically cross-reactive with native PSMA and therefore suitable for immunotherapy as it is recognized by both cellular and humoral immune responses.
 CT Check Tags: Comparative Study; Male
 Antibody Formation
 Antigens, CD3: AN, analysis
 Antigens, CD3: IM, immunology
 Antigens, CD4: AN, analysis
 Antigens, CD4: IM, immunology
 Antigens, CD8: AN, analysis
 Antigens, CD8: IM, immunology
 *Baculoviridae: CH, chemistry
 Baculoviridae: GE, genetics
 Baculoviridae: IM, immunology
 Blotting, Western
 Cell Membrane: IM, immunology
 Genetic Vectors
 Humans
 Immunity, Cellular
 Immunotherapy: MT, methods
 *Prostate-Specific Antigen: IM, immunology
 *Prostate-Specific Antigen: IP, isolation & purification
 *Prostatic Neoplasms: IM, immunology
 Prostatic Neoplasms: TH, therapy
 Protein Biosynthesis
 Recombination, Genetic
 Sensitivity and Specificity
 *T-Lymphocytes: IM, immunology
 Tumor Cells, Cultured
 CN 0 (Antigens, CD3); 0 (Antigens, CD4); 0 (Antigens, CD8); 0 (Genetic Vectors); EC 3.4.21.77 (Prostate-Specific Antigen)
 L4 ANSWER 14 OF 20 MEDLINE on STN
 AN 2000092458 MEDLINE
 DN PubMed ID: 10628836

TI PSMA mimotope isolated from phage displayed peptide library can induce PSMA specific immune response.
 AU Zhu Z Y; Zhong C P; Xu W F; Lin G M; Ye G Q; Ji Y Y; Sun B; Yeh M
 CS Shanghai Institute of Cell Biology, Chinese Academy of Sciences.
 SO Cell research, (1999 Dec) 9 (4) 271-80.
 Journal code: 9425763. ISSN: 1001-0602.
 CY China
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 200002
 ED Entered STN: 20000229
 Last Updated on STN: 20000229
 Entered Medline: 20000216
 AB Prostate-specific membrane antigen (PSMA) is a cell surface glycoprotein expressed predominantly in prostate secretory acinar epithelium and prostate cancer cells as well as in several extraprostatic tissues. Mouse monoclonal antibody 4G5 specific to the extracellular domain of PSMA was used to screen two phage displayed peptide libraries (9aa linear and 9aa cys library). Three 4G5-reactive phagotopes were identified. Sequence analysis of isolated clones demonstrated that the interaction motif "VDPA/SK" has high homology to 719-725aa on PSMA. Immunohistochemical staining of the prostate cancer sample with the PSMA-mimic phagotope (mimotope) immunized serum antibodies demonstrate that the mimotope isolated from the phage displayed peptide libraries can induce PSMA specific immune response in vivo.
 CT Check Tags: Male
 Animals
 *Antigens, Neoplasm: IM, immunology
 Antigens, Neoplasm: IP, isolation & purification
 *Antigens, Surface
 *Carboxypeptidases: IM, immunology
 Carboxypeptidases: IP, isolation & purification
 Chromatography, Affinity
 Epitopes, B-Lymphocyte: IM, immunology
 Glutamate Carboxypeptidase II
 Humans
 Mice
 Mice, Inbred C57BL
 Molecular Mimicry
 Peptide Library
 Prostate-Specific Antigen: AN, analysis
 *Prostate-Specific Antigen: IM, immunology
 Prostatic Neoplasms: CH, chemistry
 Prostatic Neoplasms: IM, immunology
 Research Support, Non-U.S. Gov't
 Sequence Analysis
 CN 0 (Antigens, Neoplasm); 0 (Antigens, Surface); 0 (Epitopes, B-Lymphocyte); 0 (Peptide Library); EC 3.4.- (Carboxypeptidases); EC 3.4.17.21 (Glutamate Carboxypeptidase II); EC 3.4.17.21 (glutamate carboxypeptidase II, human); EC 3.4.21.77 (Prostate-Specific Antigen)
 L4 ANSWER 15 OF 20 MEDLINE on STN DUPLICATE 6
 AN 1999402364 MEDLINE
 DN PubMed ID: 10475379
 TI Detection of prostatic specific membrane antigen messenger RNA using immunobead reverse transcriptase polymerase chain reaction.
 AU Ghossein R A; Osman I; Bhattacharya S; Ferrara J; Fazzari M; Cordon-Cardo C; Scher H I
 CS Department of Pathology, Memorial Sloan-Kettering Cancer Center, New York, NY 10021, USA.
 NC CA78611-02 (NCI)
 SO Diagnostic molecular pathology : American journal of surgical pathology,

part B, (1999 Jun) 8 (2) 59-65.
Journal code: 9204924. ISSN: 1052-9551.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199911

ED Entered STN: 20000111

Last Updated on STN: 20000111

Entered Medline: 19991101

AB The present study was performed to detect circulating prostatic carcinoma (PC) cells using a novel three-step immunobead reverse transcriptase (RT) polymerase chain reaction (PCR) assay for prostatic specific membrane antigen (PSMA) messenger RNA (mRNA). The sensitivity and specificity of this technique was assessed and the incidence of immunobead RT-PCR positivity correlated with progressive metastatic disease and serum prostatic specific antigen (PSA) levels. Fifty peripheral blood (PB) samples from 46 patients with PC were incubated with magnetic beads coated with Ber-EP4 antibody directed against the human epithelial antigen a membrane antigen widely expressed by epithelial cells. The epithelial cell-enriched magnetic fraction was then subjected to mRNA isolation using oligo-deoxythymidine (dT) magnetic beads. Nested RT-PCR for PSMA was performed on the mRNA oligo-dT complex and the identity of the RT-PCR products was confirmed by Southern blotting. Twenty-one PB samples from 8 control subjects without PC were also evaluated. Three-step immunobead PSMA RT-PCR was able to detect one PC cell per 1 mL of PB. The positivity rate of the RT-PCR assay was significantly higher (11 of 25; 44%) in patients with metastatic tumor than in patients with non-metastatic disease (1 of 21; 5%) ($P = 0.003$). In patients with metastatic PC, RT-PCR positivity was much higher in patients with progressive disease (10 of 13; 77%) than in patients with responding or stable disease (1 of 12; 8%) ($P = 0.001$). There was a statistically significant correlation between immunobead PSMA PCR positivity and high levels of serum PSA ($P = 0.005$). All control subjects without PC tested negative for PSMA PCR. The three-step immunobead RT-PCR for PSMA can detect circulating PC cells with high specificity and sensitivity. Preliminary data show a strong correlation between immunobead PCR positivity, the presence of progressive metastatic disease, and high levels of serum PSA.

CT Check Tags: Male

Antigens, Surface: ME, metabolism

Blotting, Southern

*Carboxypeptidases: BL, blood

Carboxypeptidases: GE, genetics

Electrophoresis, Agar Gel

Glutamate Carboxypeptidase II

Humans

Immunomagnetic Separation

Neoplasm Circulating Cells: ME, metabolism

Prostate-Specific Antigen: BL, blood

*Prostatic Neoplasms: BL, blood

Prostatic Neoplasms: DI, diagnosis

Prostatic Neoplasms: ME, metabolism

RNA, Messenger: BL, blood

Research Support, Non-U.S. Gov't

Research Support, U.S. Gov't, P.H.S.

*Reverse Transcriptase Polymerase Chain Reaction: MT, methods

Sensitivity and Specificity

Tumor Cells, Cultured

*Tumor Markers, Biological

CN 0 (Antigens, Surface); 0 (RNA, Messenger); 0 (Tumor Markers, Biological);
0 (human epithelial antigen-125); EC 3.4.- (Carboxypeptidases); EC
3.4.17.21 (Glutamate Carboxypeptidase II); EC 3.4.17.21 (glutamate
carboxypeptidase II, human); EC 3.4.21.77 (Prostate-Specific Antigen)

L4 ANSWER 16 OF 20 MEDLINE on STN
 AN 1999025849 MEDLINE
 DN PubMed ID: 9809977
 TI Identification, purification, and subcellular localization of prostate-specific membrane antigen PSM' protein in the LNCaP prostatic carcinoma cell line.
 AU Grauer L S; Lawler K D; Marignac J L; Kumar A; Goel A S; Wolfert R L
 CS Hybritech Incorporated, Beckman Coulter, Inc., San Diego, California 92196-9006, USA.
 SO Cancer research, (1998 Nov 1) 58 (21) 4787-9.
 Journal code: 2984705R. ISSN: 0008-5472.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199811
 ED Entered STN: 19990106
 Last Updated on STN: 20000303
 Entered Medline: 19981118
 AB An alternatively spliced variant of prostate-specific membrane antigen (PSMA) designated PSM' was originally described following identification of its mRNA in normal prostate. We have purified the PSM' protein from LNCaP cells using two immunoaffinity columns in tandem. The first column contained a monoclonal antibody (7E11) that was reactive with the NH2 terminus of PSMA, which specifically depleted the LNCaP lysate of full-length PSMA. The nonbinding fraction was then passed over a second column composed of a monoclonal antibody (PEQ226.5), the epitope of which was located within the 134-437 domain of PSMA and shared with PSM'. The protein eluted from the second immunoaffinity column produced a Mr 95,000 band on SDS-PAGE, which was slightly lower than the full-length PSMA at Mr 100,000. The band was NH2-terminally sequenced through 15 residues, and the assigned sequence coincided with the predicted sequence for PSM' protein minus the first two NH2 terminus amino acids. The PSM' protein, therefore, began with residue 60 of PSMA (alanine). LNCaP cells were fractionated, and PSM' was localized to the cytoplasm.
 CT Check Tags: Male
 Animals
 *Antigens, Neoplasm: IP, isolation & purification
 *Antigens, Surface
 Carboxypeptidases: AN, analysis
 Carboxypeptidases: GE, genetics
 *Carboxypeptidases: IP, isolation & purification
 Cell Membrane: CH, chemistry
 Cytoplasm: CH, chemistry
 Glutamate Carboxypeptidase II
 Humans
 Mice
 Mice, Inbred BALB C
 Molecular Weight
 *Prostatic Neoplasms: CH, chemistry
 Prostatic Neoplasms: UL, ultrastructure
 RNA, Messenger: AN, analysis
 Tumor Cells, Cultured
 CN 0 (Antigens, Neoplasm); 0 (Antigens, Surface); 0 (RNA, Messenger); EC 3.4.- (Carboxypeptidases); EC 3.4.17.21 (Glutamate Carboxypeptidase II); EC 3.4.17.21 (glutamate carboxypeptidase II, human)
 L4 ANSWER 17 OF 20 MEDLINE on STN DUPLICATE 7
 AN 1999032303 MEDLINE
 DN PubMed ID: 9817391
 TI Isolation and characterization of monoclonal antibodies specific for the extracellular domain of prostate specific membrane

antigen.

AU Murphy G P; Greene T G; Tino W T; Boynton A L; Holmes E H
 CS Northwest Hospital, Pacific Northwest Cancer Foundation and Northwest
 Biotherapeutics, Seattle, Washington, USA.
 SO Journal of urology, (1998 Dec) 160 (6 Pt 2) 2396-401.
 Journal code: 0376374. ISSN: 0022-5347.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Abridged Index Medicus Journals; Priority Journals
 EM 199812
 ED Entered STN: 19990115
 Last Updated on STN: 20000303
 Entered Medline: 19981211

AB PURPOSE: Monoclonal **antibodies** specific for protein epitopes of
 prostate specific membrane antigen (PSMA) expressed on the
 external surface of prostatic epithelial cells were prepared to provide
 material for use in the diagnosis or treatment of prostatic cancer.
 MATERIALS AND METHODS: Mice were immunized with LNCaP cell membranes
 followed by purified PSMA before fusion. Hybridomas were
 screened by reactivity with purified PSMA. Resulting
antibodies were characterized by enzyme-linked immunosorbent
 assay, Western blot and fluorescence-activated cell sorter analyses.
 RESULTS: Monoclonal antibody producing hybridomas designated
 3E11, 3C2, 4E10-1.14, 3C9 and 1G3 were obtained which displayed
 specificities for differing regions of the extracellular domain of the
 PSMA protein. These **antibodies** reacted strongly with
 PSMA from multiple sources and specifically stained unfixed
 PSMA expressing cells by flow cytometric analysis. CONCLUSIONS:
 The **antibodies** obtained displayed strong reactivity and
 specificity for extracellular epitopes of PSMA. These
antibodies will have value in future diagnostic and therapeutic
 applications focusing on PSMA as a target antigen.

CT Check Tags: Female
 Animals
 *Antibodies, Monoclonal: IP, isolation & purification
 Blotting, Western
 *Carboxypeptidases: IM, immunology
 Epitopes: IM, immunology
 Extracellular Space
 Glutamate Carboxypeptidase II
 Mice
 Mice, Inbred BALB C
 Research Support, Non-U.S. Gov't

CN 0 (Antibodies, Monoclonal); 0 (Epitopes); EC 3.4.-
 (Carboxypeptidases); EC 3.4.17.21 (Glutamate Carboxypeptidase II)

L4 ANSWER 18 OF 20 MEDLINE on STN DUPLICATE 8
 AN 1998362085 MEDLINE
 DN PubMed ID: 9694964
 TI Molecular characterization of human brain N-acetylated alpha-linked acidic
 dipeptidase (NAALADase).
 AU Luthi-Carter R; Barczak A K; Speno H; Coyle J T
 CS Laboratory of Molecular and Developmental Neuroscience, Massachusetts
 General Hospital-East, Charlestown, Massachusetts, USA.
 NC MH-572901 (NIMH)
 MH/NS-31862 (NIMH)
 SO Journal of pharmacology and experimental therapeutics, (1998 Aug) 286 (2)
 1020-5.
 Journal code: 0376362. ISSN: 0022-3565.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals

EM 199809
ED Entered STN: 19980910
Last Updated on STN: 20000303
Entered Medline: 19980902
AB N-Acetylated alpha-linked acidic dipeptidase (NAALADase) is a neuropeptidase that may modulate glutamatergic neurotransmission. Independent of its characterization in the nervous system, one form of NAALADase was shown to be expressed at high levels in human prostatic adenocarcinomas, and it was designated the prostate-specific membrane antigen (PSMA). The NAALADase/PSMA gene is known to produce multiple mRNA splice forms, and based on previous immunohistochemical evidence, it had been assumed that the human brain and prostate expressed different isoforms of the enzyme. Because PSMA is being actively pursued as a target for autoimmune and cytotoxic targeting strategies to treat prostate cancer, the rigorous comparison of the two forms of the enzyme remained an important but untested question. To assess similarities and/or differences between human brain NAALADase and PSMA, we compared the two molecules using criteria of activity, immunoreactivity and sequences of the corresponding mRNAs. NAALADase from human cerebellar isolates displayed a kinetic profile and pharmacological sensitivities similar to PSMA. Also, Northern hybridization to PSMA cDNA detected indistinguishable sets of 2.8-, 4.0- and 6.0-kb RNA species in human brain and the LNCaP prostatic tumor cell line. In addition, the monoclonal antibody 7E11-C5 directed against the prostatic form of the enzyme immunoprecipitated 82% of human cerebellar NAALADase activity. Moreover, reverse transcription-polymerase chain reaction cloning of cerebellar cDNAs indicated that the human brain and prostate express a common mRNA splice form. Therefore, we conclude that the form of NAALADase also known as PSMA is expressed in brain and comprises a significant fraction of brain NAALADase activity.

CT *Antigens, Surface: ME, metabolism
Blotting, Northern
*Brain: EN, enzymology
*Carboxypeptidases: ME, metabolism
Cell Line
Cloning, Molecular
Glutamate Carboxypeptidase II
Humans
Kinetics
Polymerase Chain Reaction
Precipitin Tests
RNA, Messenger: BI, biosynthesis
RNA, Messenger: CH, chemistry
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, P.H.S.

CN 0 (Antigens, Surface); 0 (RNA, Messenger); EC 3.4.- (Carboxypeptidases); EC 3.4.17.21 (Glutamate Carboxypeptidase II); EC 3.4.17.21 (glutamate carboxypeptidase II, human)

L4 ANSWER 19 OF 20 MEDLINE on STN DUPLICATE 9
AN 1999006617 MEDLINE
DN PubMed ID: 9792131
TI Prostate cancer and prostate bed SPECT imaging with ProstaScint: semiquantitative correlation with prostatic biopsy results.
AU Sodee D B; Ellis R J; Samuels M A; Spirnak J P; Poole W F; Riester C; Martanovic D M; Stonecipher R; Bellon E M
CS Department of Radiology, MetroHealth Medical Center/Case Western Reserve University, Cleveland, Ohio, USA.
SO Prostate, (1998 Nov 1) 37 (3) 140-8.
Journal code: 8101368. ISSN: 0270-4137.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English

FS Priority Journals
 EM 199811
 ED Entered STN: 19990106
 Last Updated on STN: 19990106
 Entered Medline: 19981112
 AB BACKGROUND: ProstaScint (Cytogen Corporation, Princeton, NJ) murine monoclonal antibody imaging is FDA-approved for imaging of prostate cancer patients at high risk for metastatic disease and patients postprostatectomy with a rising serum prostate-specific antigen (PSA) level. ProstaScint is a murine monoclonal antibody which targets prostate-specific membrane antigen (PSMA). PSMA expression is upregulated in primary and metastatic prostate cancer. FDA Cytogen (Princeton, NJ) protocol studies using 111indium-labeled ProstaScint revealed correlation between areas of increased concentration in the prostate and biopsy-proven tumors in patients imaged pretherapy. METHODS: In our study, four transverse, single-photon emission tomography (SPECT) images were isolated and regions of interest were selected and correlated with pretherapy prostate biopsy results. Prostate cancer and normal tissue prostate/muscle background (P/M) ratios were derived, so that postprostatectomy/radiation therapy patients could be evaluated for the presence of residual prostate cancer. Twenty-three pretherapy prostate cancer patients with quadrant/sextant biopsies had SPECT 96-hr 111indium ProstaScint pelvic images. The four transverse 1-cm slices above the midline penile blood pool were chosen, and four to six 27-30-pixel regions of interest were placed over the prostate bed. The background muscle region of interest was placed over the external obturator muscle region. The P/M ratio was calculated and compared to the quadrant/sextant prostatic biopsy result. The same procedure was applied to 17 posttherapy prostate cancer patients with rising PSA. RESULTS: In the 23 pretherapy prostate cancer patients, there was a correlation between the P/M ratio of at least 3.0 in 32 of 35 prostatic cancer biopsy regions, and there was correlation with P/M ratios less than 3.0 in 82 of 89 negative biopsy regions. Seventeen posttherapy patients underwent ProstaScint studies. Six underwent biopsy, with typically one biopsy site per patient. All 6 had P/M ratios greater than 3.0 in the biopsied region. Five out of six biopsies revealed residual prostate cancer. CONCLUSIONS: A prostate/muscle ratio was developed from 111indium ProstaScint regions of interest obtained on 1-cm SPECT transverse slices through the prostate bed in 23 patients preprostatic cancer therapy. A P/M ratio above 3.0 correlated in the majority of positive cases, and a P/M ratio below 3.0 was demonstrated in negative prostatic biopsy cases. The P/M ratio of above 3.0 or below 3.0 also separated those posttherapy prostate cancer patients with rising PSA who had residual prostate carcinoma in the prostate bed.
 CT Check Tags: Male
 Aged
 Antibodies, Monoclonal: DU, diagnostic use
 Biopsy
 Humans
 Indium Radioisotopes: DU, diagnostic use
 Middle Aged
 *Prostate: PA, pathology
 Prostate-Specific Antigen: IM, immunology
 Prostatic Neoplasms: PA, pathology
 *Prostatic Neoplasms: RI, radionuclide imaging
 *Tomography, Emission-Computed, Single-Photon: MT, methods
 CN 0 (Antibodies, Monoclonal); 0 (Indium Radioisotopes); EC
 3.4.21.77 (Prostate-Specific Antigen)
 L4 ANSWER 20 OF 20 MEDLINE on STN DUPLICATE 10
 AN 96186631 MEDLINE
 DN PubMed ID: 8602402
 TI Measurement of prostate-specific membrane antigen in the serum with a new antibody.

AU ~~Murphy~~ G P; Tino W T; Holmes E H; Boynton A L; Erickson S J; Bowes V A;
 Barren R J; Tjoa B A; Misrock S L; Ragde H; Kenny G M
 CS Pacific Northwest Cancer Foundation, Cancer Research Division, Northwest
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 SO Prostate, (1996 Apr) 28(4): 266-71.
 Journal code: 8101368. ISSN: 0270-4137.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199605
 ED Entered STN: 19960517
 Last Updated on STN: 19970203
 Entered Medline: 19960503
 AB Work to date has identified prostate-specific membrane antigen (**PSMA**) as a membrane-bound glycoprotein with high specificity for prostatic epithelial cells. **PSMA** reacts with the monoclonal antibody 7E11.C5, which is present in serum, seminal fluid, and prostatic epithelial cells, and is increased in its expression in the presence of a hormone refractory state associated with prostatic cancer. This report confirms these results and further documents the presence of the monoclonal antibody 3F5.4G6, which reacts with the extracellular domain of **PSMA**. This region of **PSMA** is also an element present in a truncated version of the protein, so-called **PSM'**. Immune precipitation with either 7E11.C5 or 3F5.4G6 yields an isolated protein species that are reactive with the reciprocal antibody in Western blot analysis. Thus, 3F5.4G6 recognizes the same **PSMA** protein as does 7E11.C5, but at different epitopes on essentially opposite ends of the molecule. These two antibodies are well suited for use in a sandwich immunoassay, either one as a capture or detection antibody. Current work on this is underway. This report also confirms that 7E11.C5 Western blots for **PSMA** are negative with normal human brain tissue. The monoclonal antibody 9H10 does not react with 3F5.4G6 or with 7E11.C5 in studies conducted herein. Moreover, 3F5.4G6 reacts with **PSMA** found in the LNCaP cell line, but not DU-145 or PC3, which lack **PSMA**.
 CT Check Tags: Male
 Amino Acid Sequence
 Animals
 Antibodies, Monoclonal: AN, analysis
 *Antibodies, Monoclonal: IM, immunology
 Antibodies, Monoclonal: IP, isolation & purification
 Blotting, Western: MT, methods
 Humans
 Hybridomas
 Mice
 Mice, Inbred BALB C
 Molecular Sequence Data
 Multiple Myeloma: PA, pathology
 Precipitin Tests
 *Prostate-Specific Antigen: BL, blood
 Prostate-Specific Antigen: CH, chemistry
 Prostate-Specific Antigen: IM, immunology
 Prostatic Neoplasms: PA, pathology
 Radioimmunoassay: MT, methods
 Research Support, Non-U.S. Gov't
 Tumor Cells, Cultured
 CN 0 (Antibodies, Monoclonal); EC 3.4.21.77 (Prostate-Specific Antigen)